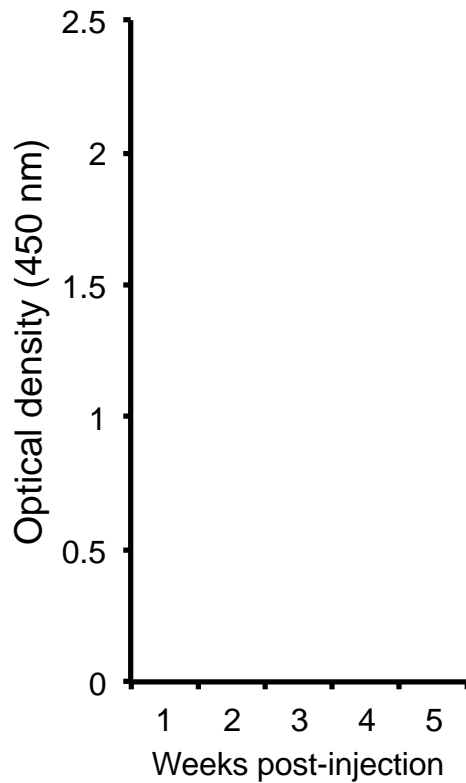
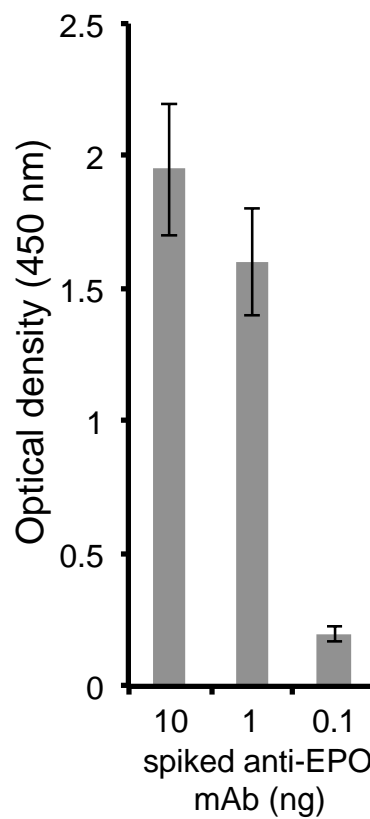


Supplementary Figure 1 Intravenously administered mRNA-LNPs target the liver. Representative IVIS image (24 hours post-injection) of BALB/c mice injected with 5 μ g LNP-complexed firefly luciferase-encoding mRNA by the intravenous route.

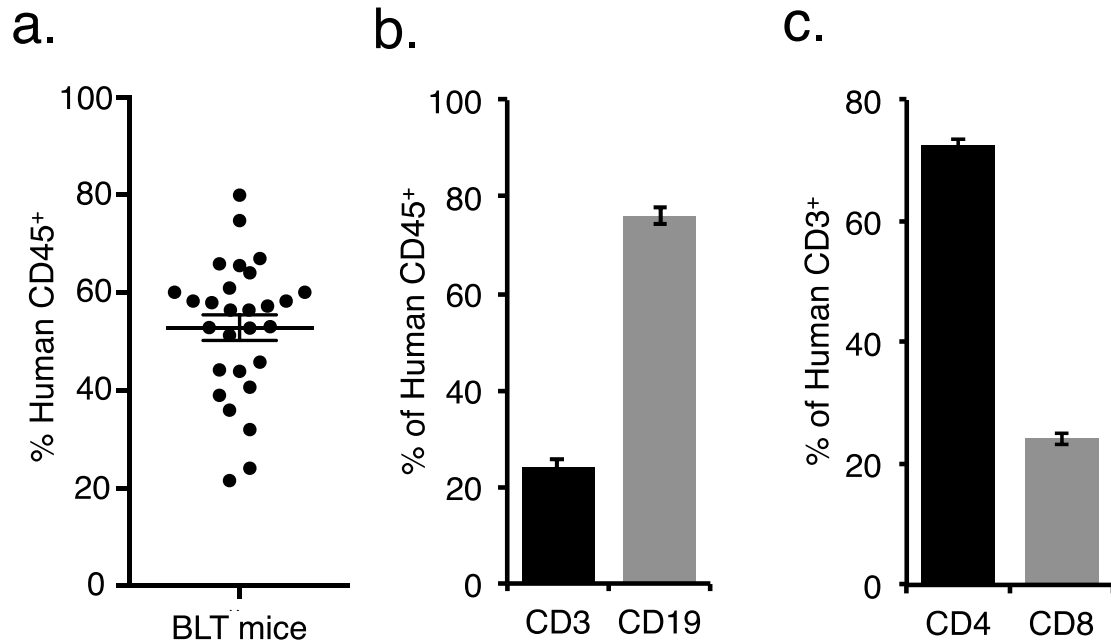
a.



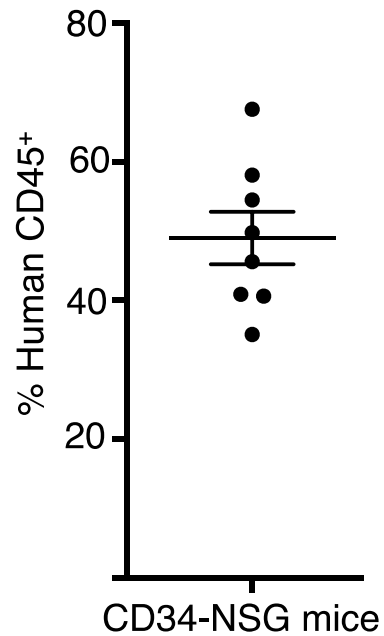
b.



Supplementary Figure 2 Repeated delivery of nucleoside-modified mRNA into immunocompetent mice. BALB/c mice were intraperitoneally injected weekly for 5 weeks with 0.1 μ g of murine erythropoietin (muEPO) encoding nucleoside-modified mRNA. **(a)** Animals were bled 1 week after each injection and antibody responses to muEPO protein were measured in the plasma by ELISA. **(b)** To measure the sensitivity of the ELISA, recombinant anti-muEPO antibodies (10, 1 and 0.1 ng) were spiked into mouse plasma and analyzed. Group size is 5 animals.



Supplementary Figure 3 Characterization of BLT humanized mice. BLT humanized mice were engrafted with 100,000 CD34⁺ human hematopoietic stem cells. **(a)** Chimerism was measured in peripheral blood 16 weeks later by enumerating human CD45⁺ cells in blood. **(b)** Percent of T cells (CD3⁺) and B cells (CD19⁺) of CD45⁺ cells in BLT mice. **(c)** Percent of CD4⁺ and CD8⁺ T cells of total CD3⁺ T cells in BLT mice. Group size is 28 animals.



Supplementary Figure 4 Characterization of humanized CD34-NSG mice.

NSG humanized mice were engrafted with 100,000 CD34⁺ human hematopoietic stem cells. Chimerism was measured in peripheral blood 12 weeks later by enumerating human CD45⁺ cells in blood. Group size is 8 animals.